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Stenting for pulmonary artery stenosis complicated by univentricular physiology: Subanalysis of JPIC stent survey

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ABSTRACT

Background and purpose: Stent implantation is an important treatment option for pulmonary artery stenosis (PS), even if complicated by univentricular physiology (UVP). However, there is paucity of evidence concerning not only its hemodynamic and morphologic indications but also on markers for its optimal target attainment in UVP. The purpose of this study was to evaluate the acute outcome and factors associated with efficacy of stenting for PS complicating UVP.

Methods and subjects: A subanalysis was performed using the data of the Japanese Society of Pediatric Interventional Cardiology (JPIC) stent survey. We analyzed the morphologic and hemodynamic data of 11 patients with UVP who underwent stenting for PS. We defined "a 50% increase in the minimum lumen diameter (MLD)" as "morphologically effective," and "an achievement of 0 mmHg pressure gradient" as "hemodynamically effective." We analyzed the success rate for each criterion and determined factors which may have contributed to hemodynamic effectiveness.

Results: Stenting was morphologically effective in all patients, while it was hemodynamically effective in 6/11 (55%). The percent diameter stenosis after stenting was significantly lower in the "hemodynamically effective" group ($2.5 \pm 5.5\%$ vs $19.6 \pm 13.1\%$, $p = 0.017$). The cutoff value of percent diameter stenosis after stenting to "hemodynamically effective" was 14.6%; the sensitivity was 80% and the specificity was 100% (area under the curve 0.825, $p = 0.021$).

Conclusions: The percent diameter stenosis after stenting significantly contributed to achieving a "0 mmHg" pressure gradient, while in order to achieve a "0 mmHg" pressure gradient, the residual percent diameter stenosis should be less than around 15%.

Introduction

The Fontan operation has contributed to improved survival of patients with univentricular physiology (UVP); concurrently, after its first description in 1989 [1,2], the use of metallic stents for pulmonary arterial stenosis (PS) in congenital heart disease has become an important option for treating PS even in patients with UVP. PS in such patients may be attributed to anatomical and surgical risk associated with growth failure of a segment of the native vessel, external compression by anatomic structures, and an inadequate patching at a previous operation. Consequently, catheter intervention is a reasonable approach to relieve stenosis affecting such low pressure systems. The increasing number of Fontan patients under follow-up means an increased number of potential cardiac catheterization and interventional procedure candidates. These procedures may be an important component of staged surgical palliation for univentricular heart, especially in the management of PS requiring prompt intervention. Intervention may allow high-risk surgical repair to be deferred or may even replace it. However, little has been written about stent implantation

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in patients with univentricular heart, and factors associated with successful stent implantation for PS in these patients, while outcomes of this situation have not been published. Thus, accurately identifying the optimal stent diameter implanted for PS may be crucially important for patients with UVP. The purpose of this study was to evaluate the acute outcome and factors associated with efficacy of stenting for PS complicating UVP.

Methods

A subanalysis was performed from the data of the Japanese Society of Pediatric Interventional Cardiology (JPIC) stent survey, which is a retrospective questionnaire-based survey of stenting for congenital heart diseases from May 1995 to February 2009 at 14 leading hospitals in Japan [3]. We retrospectively analyzed the impact of stent implantation for treatment of PS in patients with UVP undertaken to optimize the circulation, with special attention to morphologic and hemodynamic effectiveness, and factors that may have contributed to its effectiveness. We analyzed morphologic and hemodynamic data of patients with UVP, who underwent stenting for PS associated with a mean pressure gradient of at least 1 mmHg. Patients who had morphologic stenosis but no measurable pressure gradient across the stenosis were excluded. For analysis, 11 patients who received at least one stent implantation for PS after a bidirectional Glenn or Fontan operation were enrolled. We defined "a 50% increase in the minimum lumen diameter (MLD)" as "morphologically effective" [4], and "an achievement of 0 mmHg pressure gradient" as "hemodynamically effective." Each criterion was examined. Furthermore, we analyzed factors that may have contributed to hemodynamic effectiveness, including MLD, reference vessel diameter (RVD), mean pressure gradient through the target lesion before and after stenting, and balloon diameter used for deployment. Percent increase in MLD and percent diameter stenosis (%DS) were defined as [(MLD after − MLD before)/MLD before] and [(RVD − MLD)/RVD], respectively. If the MLD after stent is larger than RVD, %DS becomes a negative value; we treated the negative value as "0%" for the analysis, because the negative value of %DS does not have a practical meaning. Each data point was expressed as a mean value ± SD. The values between the "effective" and "non-effective" groups were also compared. The Student's *t*-test was used to compare means between each group. The cutoff value was evaluated using receiver operating characteristic (ROC) curve of factors which contributed to effective stenting. Statistical analyses were performed with the statistical software package JMP® 10 (SAS Institute Inc., Cary, NC, USA).

Results

From May 1995 to February 2009, 31 patients with UVP underwent stent implantation. In 11 of them (3 after Fontan operation and 8 after bidirectional Glenn operation), a stent was implanted to treat PS with a measurable pressure gradient. The patient profiles are summarized in Table 1. The median age of the patients at catheterization was 2.0 (0.8–20.0) years. The original Palmaz stent was used in 10 patients (extra-large, 1; large, 4; medium, 5) and a Palmaz Genesis stent in one patient. Stents were deployed using standard techniques. Morphologic and hemodynamic parameters, before and after stenting, are presented in Table 2. As mentioned above, we treated the negative value of %DS as "0%". Stent implantation resulted in a significant reduction of the pressure gradient and %DS in the majority of our patients. Stenting was morphologically effective in all patients, while it was hemodynamically effective in 6/11 (55%) patients. The comparisons of parameters in the two groups (hemodynamically "effective" and "non-effective") are summarized in Table 3. The %DS after stenting was significantly lower in the "hemodynamically effective" group than in the "non-effective" group (2.5 ± 5.5% vs 19.6 ± 13.1%, $p = 0.017$) (Fig. 1). The cutoff value of %DS after stenting to "hemodynamically effective" was 14.6%; the sensitivity was 80% and the specificity was 100% (area under the curve 0.825, $p = 0.021$) (Fig. 2).

Table 1
Patients' profile (basic diagnosis and type of operation).

No.	Age	Sex	Basic diagnosis	Type of operation
1	0.8	Female	Ebstein, PA	BDG
2	1.0	Male	HLHS	BDG
3	1.0	Male	HLHS	BDG
4	1.0	Male	SRV	BDG
5	2.0	Male	HLHS	Fontan
6	2.0	Male	PA/IVS	Fontan
7	4.0	Male	HLHS	BDG
8	8.0	Female	TA	BDG
9	8.0	Female	DORV, PA	Fontan
10	17.0	Female	TA	BDG
11	20.0	Female	AVSD	BDG

PA, pulmonary atresia; HLHS, hypoplastic left heart syndrome; SRV, single right ventricle; PA/IVS, pulmonary atresia with intact atrial septum; TA, tricuspid atresia; DORV, double outlet right ventricle; AVSD, atrioventricular septal defect; BDG, bidirectional Glenn.

Discussion

PS complicating UVP may lead to various morbidities, including changes in the pulmonary vascular bed, increased central venous pressure, ascites, pleural effusion, and protein losing enteropathy. The long-term outcome after bidirectional Glenn and Fontan procedures depends on pulmonary artery growth [5]. In these patients, the pulmonary circulation lacks a pumping chamber and pulmonary blood flow is driven by systemic venous pressure. Unobstructed pulmonary blood flow in a univentricular circulation is a major determinant of a good long-term outcome, and in relieving PS

Table 2
Morphologic and hemodynamic parameters, before and after stenting.

No.	Type of stent	Before stent			After stent			RVD	% change in MLD
		MLD	%DS	Mean PG	MLD	%DS	Mean PG		
1	P1506	2.1	73.8	4.0	5.3	33.8	3.0	8.0	152.4
2	P2006	2.2	60.0	1.0	5.4	1.8	0.0	5.5	145.5
3	P2007	3.8	32.1	1.0	6.3	0	0.0	5.6	65.8
4	PG2980	3.9	58.1	1.0	7.4	20.4	1.0	9.3	89.7
5	P2007	3.8	34.5	3.0	6.6	0	0.0	5.8	73.7
6	P2007	4.1	43.8	2.0	6.3	13.7	0.0	7.3	53.7
7	P3008	4.0	40.3	4.0	7.3	0	1.0	6.7	82.5
8	P3008	2.0	79.2	3.0	10.0	0	0.0	9.6	400.0
9	P4010	5.3	33.8	2.0	8.2	0	0.0	8.0	54.7
10	P3008	4.4	47.6	9.0	7.1	15.5	6.0	8.4	61.4
11	P3008	4.7	63.8	2.0	9.3	28.5	1.0	13.0	97.9

MLD, minimum lumen diameter; %DS, percent diameter stenosis; PG, pressure gradient; RVD, reference vessel diameter.

Table 3
Comparisons of morphologic and hemodynamic parameters in the two groups.

Parameter	"Effective" group $N=6$	"Non-effective" group $N=5$	p value
Before stent			
MLD	3.5 ± 1.2	3.8 ± 1.0	NS
%DS	47.2 ± 18.8	54.7 ± 10.4	NS
Mean PG	2.0 ± 0.9	4.0 ± 3.1	NS
After stent			
MLD	7.1 ± 1.7	7.2 ± 1.4	NS
%DS	2.6 ± 5.5	19.6 ± 13.1	0.017
RVD	7.0 ± 1.6	8.6 ± 3.0	NS
% change in MLD	132.2 ± 135.6	96.8 ± 33.9	NS

MLD, minimum lumen diameter; %DS, percent diameter stenosis; PG, pressure gradient; RVD, reference vessel diameter.

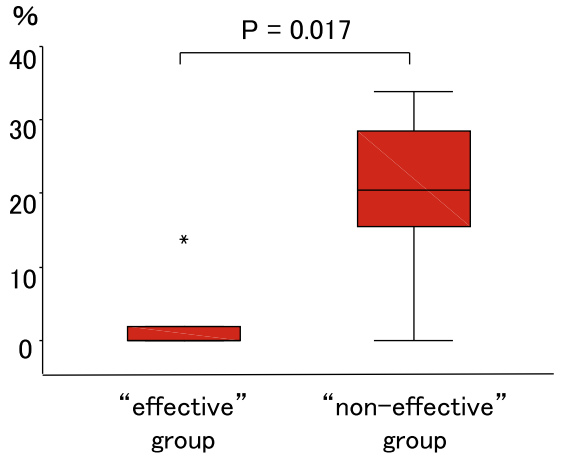

Fig. 1. The percent diameter stenosis of two groups (hemodynamically "effective" and "non-effective").

in these patients it is important to optimize the long-term hemodynamics. Even mild stenosis might result in further suboptimal pulmonary artery growth and deterioration of systemic venous hemodynamics [5], and these lesions may become clinically significant even in the absence of a measurable pressure gradient in this low-pressure system [6]. Many aspects of liver function may be impaired by the chronic systemic venous hypertension. However, there are few reports of stent therapy for PS of UVP [7–14].

Kretschmar et al. [14] described their experience with stent implantation for PS in children with UVP before and after completion of partial and total cavopulmonary connections (TCPC). They implanted 17 stents for PS in 12 patients before and after TCPC.

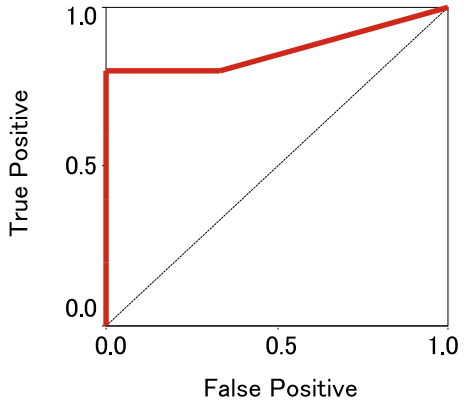

Fig. 2. Receiver operating characteristics curve of percent diameter stenosis to "0 mmHg" pressure gradient.

PS was treated effectively and safely, while the pressure gradient was not completely abolished but decreased from 7.1 ± 6.1 mmHg (0–20 mmHg) to 1.2 ± 2.2 mmHg. They did not calculate the optimal stent size for complete reduction of the pressure gradient. Moszura et al. [9] also reported their results of stenting for postoperative PS as a part of multistage treatment for hypoplastic left heart syndrome. Stenting for PS was performed in 16 patients (28% of the patients) after bidirectional Glenn and made up the predominant intervention in their cohort. Pulmonary artery pressure was reduced and the diameter of the stented vessel was increased (from a mean of 15.56 ± 6.85 mmHg to a mean of 13 ± 5.35 mmHg, and from a mean of 4.56 ± 1.17 mm to a mean of 9 ± 1.73 mm). They described how stent implantation into narrowed pulmonary arteries allowed for improving suitability for the Fontan operation; however, clear standards for indications and effectiveness for stent implantation in terms of %DS and pressure gradient were not shown. Ovroutski et al. [10] reported 20 interventions for reduction of stenosis in the Fontan pathway in 14 patients. Six of them were stent implantations for PS. They showed that relief of stenosis can effectively improve the hemodynamics in the Fontan circulation, even in patients without a measurable pressure gradient. They speculated that morphologic narrowing without a significant pressure gradient may be difficult to ascertain precisely in the low-pressure system, and might also hinder passive venous flow, especially in the direction opposite to gravity. They recommended a percutaneous approach even in cases where the obstruction is angiographically mild with no significant pressure gradient.

Stenting in the Fontan route was also applied to the extra cardiac (EC) conduit or lateral tunnel (LT) pathway [6,13,15,16]. Ewert et al. [13] reported the retrospective analysis of 60 implanted CP stents including six cases of TCPC. A residual pressure gradient of 4 mmHg after attempted balloon dilatation and morphological stenosis without pressure gradient were the criteria for stent placement. Six stents were placed in caval veins and EC conduits and pressure gradients dropped from 4 mmHg (range 4–20 mmHg) to 0 mmHg (range 0–3 mmHg). Although, not intended for the pulmonary artery, this study is similar to our study from the point of view of targeting the low-pressure system in a Fontan type circulation. Mets et al. [6] also described their experience with stent implantation for obstruction of intracardiac LT Fontan pathways. Fifty-one patients underwent stent implantation for LT pathway stenosis. These patients had significantly higher inferior vena cava pressures than controls, but only 35% had a measurable pressure gradient in the catheterization laboratory. Stenting increased the mean diameter of the LT stenosis with few adverse events and eliminated the pressure gradient when present. However, we may not always be able to achieve enough % diameter decrease in stenosis in PS, because of its complex anatomy in contrast to the relatively straight EC conduit or LT stenosis.

The magnitude of resistance in the venous system of Fontan patients tends to be underestimated during catheterization, because catheterization is performed under resting conditions or under sedation or general anesthesia [6]. Therefore, a measurable pressure gradient across the stenosis is significant from the point of view of energy loss, and achievement of "0 mmHg" pressure gradient of the pulmonary stenosis derived from stent implantation is beneficial [6]. Although the optimal size of stent for PS in UVP is unknown, we consider it is likely to be large if required to achieve "0 mmHg" pressure gradient. According to our study, "0 mmHg" pressure gradient of the pulmonary stenosis is likely to be achieved in patients with UVP if residual %DS is less than around 15%, and this seems to be a reasonable target. Our data are incomplete and we are unable to determine clinical benefit, so the clinical implications of stenting for PS of UVP and target size for stenting deserve further investigation.

Limitations

This study is based on data from a questionnaire survey, and is limited to the background data of the patients, morphological measurement of the target, and pressure gradients. Lack of other hemodynamic data such as central venous pressure and arterial oxygen saturation limits the analysis. Consequently, this study has strong selection bias because of excluding patients with a "0 mmHg" pressure gradient even if they had morphological narrowing. Furthermore, there are no data on definitive clinical benefits related to stenting for PS in patients with UVP. The small number of patients may limit the significance of statistical analysis. However, as assessment of the benefits of stenting for PS in the low-pressure cavopulmonary system is still unclear, we believe it will be beneficial to achieve "0 mmHg" pressure gradient at rest during catheterization.

Conclusion

Although stenting was morphologically effective in all patients, "0 mmHg" pressure gradient was achieved only in 55%. The %DS after stenting significantly contributed to achieving "0 mmHg" pressure gradient, while in order to achieve "0 mmHg" pressure gradient, residual %DS should be less than around 15% in patients with univentricular physiology complicated by pulmonary stenosis.

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